A STUDY OF THE MECHANISM OF ANOMALOUS CLEMMENSEN REDUCTIONS

BY

ROBERT CLAIR SENTZ

B.S., Bucknell University, 1948
M.S., University of Illinois, 1949

AN ABSTRACT OF A THESIS

SUBMITTED IN PARTIAL FULFILLMENT OF THE REQUIREMENTS
FOR THE DEGREE OF DOCTOR OF PHILOSOPHY IN CHEMISTRY
IN THE GRADUATE COLLEGE OF THE
UNIVERSITY OF ILLINOIS, 1952

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A STUDY OF THE MECHANISM OF ANOMALOUS CLEMMENSEN REDUCTIONS

Introduction

The rearrangement of cyclic α-aminoketones under Clemmensen reduction conditions has been shown to be a general reaction (1), but the mechanism of the rearrangement has not been elucidated satisfactorily. Since the rearrangement is probably a multistep process, it would be advantageous to discover the nature of the individual steps. In the strongly acid medium, the most likely alternatives for the initial step in the rearrangement sequence have been considered to be (a) C_α-N cleavage (2), and (b) a concerted intramolecular rearrangement involving hydride attack at the α-carbon (3). There are two attractive approaches which would enable one to come to a decision between these alternatives. One would be to use a cyclic α-aminoketone of such ring size that an open-chain product would be formed if process (a) is followed, or a ring-contracted product if the rearrangement is concerted. A second approach would be to investigate the fate of asymmetry at the α-carbon, since optical activity would be lost or retained in the rearranged product if the reaction proceeded by process (a) or (b), respectively. The present investigation describes the synthesis and the Clemmensen reduction of an eight-membered-ring α-aminoketone.

Discussion of Results

It has been shown that an eight-membered-ring α-aminoketone in which the carbonyl and amine groups are homocyclic undergoes C_α-N Cleavage under Clemmensen reduction conditions, and that an open chain structure results. Specifically, the reduction of 1,2-dimethyl-1-azacycloöctan-3-one with zinc amalgam and hydrochloric acid yields N-methyloctylamine. For the synthesis of 1,2-dimethyl-1-azacycloöctan-3-one, the Dieckmann ring closure of α-carbethoxyethyl-ε-carbethoxy-

pentylmethylamine was employed under conditions of high dilution, with potassium *t*-butoxide as the condensing agent. This appears to be the first successful application of the Dieckmann reaction to the closure of an eight-membered ring. The Dieckmann ring closure, modified as to condensing agent, solvent and dilution, and certain related theoretical considerations have been discussed. Conclusions have been drawn regarding the optimum conditions for the Dieckmann synthesis of large rings in general.

The Wolff-Kishner reduction of 1,2-dimethyl-1-azacycloöctan-3-one has been found to proceed anomalously to give N-methyloctenylamine rather than the expected 1,2-dimethyl-1-azacycloöctane. This has led to a new concept of the Wolff-Kishner reduction of certain α-substituted ketones.

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VITA

The author was born in Red Lion, Pennsylvania, on October 1, 1922. He graduated from Red Lion High School in 1940, and entered West Chester State Teachers College in September of that year. From March, 1943 to April, 1946 he served in the Army of the United States. During this time three terms were spent in the advanced Army Specialized Training Program at the University of West Virginia. Upon discharge from the Army, he enrolled at Bucknell University where he received the degree of Bachelor of Science in Chemistry, with honors, in June, 1948. In September of that year he entered the Graduate College of the University of Illinois, and received the degree of Master of Science in June, 1949. He held University Fellowships during the academic years 1948-1949, 1950-1951, a W. P. B. Fellowship during the academic year 1949-1950, and received a grant from E. I. duPont de Nemours and Company during the summer and fall of 1951. During the summers of 1948 and 1949 he was employed by the Sun Oil Company at Norwood, Pennsylvania.